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RADIUM

EDITED BY
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VOL. VII AUGUST, 1916 No. 5

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY
PHYSICS AND THERAPEUTICS OF RADIUM
AND RADIO-ACTIVE SUBSTANCES

RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D. with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. VII. AUGUST, 1916 No. 5

EXOPHTHALMIC GOITRE*
WITH SPECIAL REFERENCE TO THE ETIOLOGY AND TREATMENT WITH RADIUM.

By W. H. B. Aikins, M.D., Toronto, Ont.

Exophthalmic goitre is referred to in literature under several different names, including Graves's disease, Basedow's disease, and Parry's disease, and the designation of hyperthyroidism has recently been applied to it by some observers. This latter term, however, can scarcely be regarded as an appropriate one, as it is now generally assumed that hyperthyroidism, although it probably plays a certain role in the causation of the disease, is not by any means the only etiological factor. The designation of exophthalmic goitre also has the disadvantage that the assumption on which it is based, namely, that exophthalmos and enlargement of the thyroid are invariably present, has now been shown to be without foundation, as one or both of these symptoms may be absent in an otherwise typical case; but it has been so generally adopted that I propose to use it.

In spite of the fact that there is probably no condition in regard to which such extensive investigations, both clinical and experimental, have been made during the last few years, and notwithstanding the amount of literature which has accumulated upon the subject, the etiology of exophthalmic goitre still remains obscure, although considerable light has been thrown upon it. The two chief theories which have been advanced may be considered under the following headings: 1. The glandular theory; 2, the neurogenic theory.

*New York Medical Journal, Vol. CIV, pp. 49-53, 1916; also Canadian Practioner and Review, August, 1916.

1. *The Glandular Theory.* The theory of Mœbius was for a long time very generally accepted as a sufficient explanation of the symptoms of exophthalmic goitre. It assumes that it is due to a primary functional disturbance of the thyroid, resulting in the production of an excess of secretion, which saturates the organism, and causes the symptom complex. Many writers now consider it probable that abnormalities of the other endocrinous glands, such as the thymus, suprarenals, hypophysis and ovary, also play a more or less important part in the etiology of the condition.

2. *The Neurogenic Theory.* The neurogenic theory does not negative the glandular theory, but is complementary to it, there still being difference of opinion whether the glandular or the neurogenous disturbance is to be regarded as the primary one. Feeding with thyroid substance, both experimentally and by the administration of thyroid tablets in man, sometimes produces the typical symptoms, while in other cases it fails to do so, even if continued for a prolonged period. This indicates that the disease cannot be regarded as a pure hyperthyroidism, but that, in addition to an abnormal secretory function of the thyroid, a predisposing factor of some kind is essential, and the facts which are now at our disposal lead to the assumption that this predisposing factor is to be sought for in a primary defect or injury to the central nervous system. This hypothesis is confirmed by the comparative frequency of the disease in neurotic persons and those with a neuropathic heredity, as manifested by the occurrence of diseases such as insanity, hysteria or epilepsy in other members of the patient's family. The predominance of symptoms referable to the nervous system in the clinical picture is also confirmatory. Bumsted (1) emphasizes that fact that direct inheritance of the disease itself is not so uncommon as is generally supposed. He cites Rosenberg's case, in which the patient's grandmother, father, two aunts, and two sisters had suffered from exophthalmic goitre, and Oesterreicher's statement that in a family of ten children eight suffered. Bumsted himself has had four sisters under his observation during the last five years. Two of them have severe exophthalmic goitre and a third early symptoms, while the fourth manifested symptoms when she had been for some time at home with her sisters after leaving school.

Although it has not yet been definitely proved, it appears probable that abnormalities of the other endocrinous glands play a part in the production of the symptoms. This applies more especially to persistence and hyperplasia of the thymus, which has been observed in a large proportion of the cases which have been examined post morthem, and is described by the French writers as rejuvenescence of the thymus. Capelle and Bayer (2) found enlargement of the gland in forty-three of sixty autopsies (seventy per cent.), Matti (3) in seventy-five per cent. of 133 autopsies, Berry (4) in 100 per cent. of the autopsies that he has made, and Klose (5) goes so far as to say that exophthalmic goitre never occurs without enlargement of the thymus. Capelle and Bayer believe that in most cases the symptoms result from abnormal function of the thyroid, which is supplied by the sympathetic nervous system, and the thymus which is supplied by the vagus. Some writers explain the symptoms, not by disease of the thyroid, but of the thymus, and Garre (6), who now operates on the thymus in every case, states that its removal causes the disappearance of Garre's characteristic blood picture. Hart (7) is inclined to agree with this opinion, and believes that the thymus of itself is capable of causing the symptoms usually

ascribed to the thyroid. He therefore assumes secondary disease of the thyroid, due partially to persistence of the thymus and partially to constitutional anomalies, above all, lesions of the nervous system. On the other hand, Kocher (8) says there is no proof that typical exophthalmic goitre can be induced by the thymus alone without hypersecretion of the thyroid, but that it is possible that hyperplasia and persistence of the thymus predispose to it. He finds that an enlarged and persistent thymus is particularly common in certain districts and certain families, in which it is seen both with and without symptoms of exophthalmic goitre. He accordingly regards it as merely a regional familial late involution, dependent upon congenital or possibly constitutional peculiarities, and not as a direct cause of the disease.

There seems reason to believe that other internal secretion glands have some influence. In exophthalmic goitre Kocher found general hyperplasia of the lymphoid organs and proliferation of ectopic lymphoid tissue, involving the suprarenals, and ovaries, and more rarely the pancreas. The frequency of pigmentation of the skin suggests the possibility of an influence of the suprarenals, while the greater frequency of the disease in women points to the influence of ovarian secretion. It is a well known fact that there is a predisposition to the onset of exophthalmic goitre at puberty and the cessation of menstruation, and to exacerbations of the already existing disease during menstruation and pregnancy.

While there is evidence that an excess of thyroid secretion is of importance in giving rise to the symptoms of exophthalmic goitre, there seems reason to believe that it does so only if some predisposing factor is present, and that this primary predisposing factor consists in an injury to the nervous system. The secretion of the thyroid gland consists of iodine, an albumin body, and a group of proteins, and described collectively as iodothyreoglobulin. This combination appears to possess specific characteristics, which none of its constituents possesses in itself, either alone or in combination with one of the others. Oswald, who has made extensive investigations in this connection, states that iodothyreoglobulin increases nerve tonus and the excitability of the nervous system, and also favors metabolism and degeneration of the albumin and fat. These properties explain the clinical pictures of myxedema and hyperthyroidism, thyroid secretion in the former being reduced or abolished, and in the latter increased. Oswald (9) points out the significance of the fact that symptoms of exophthalmic goitre do not invariably develop in response to saturation of the organism with iodothyreoglobulin, and therefore concludes that the exothyroid contributory factor must be something more than a mere predisposition. Oswald does not regard the saturation of the organism with iodothyreoglobulin as primary, but as a result of increased innervation of the gland and excessive flow of blood through it, in which the nervous system plays the primary role. A so called vicious circle is thus established, the excessive amount of secretion poured out increasing still further the tonus and excitability of the nervous system, and the latter in its turn reacting on the thyroid, and intensifying its innervation and thereby its secretory activity.

Constitutional diseases, such as diabetes, gout, and obesity, are not infrequently present in these cases, and careful inquiry will often elicit the information that the patient has for a long time suffered from servere nervous and psychical disorders, sometimes dating back to childhood.

We find that long before the appearance of the typical symptoms the patient has been nervous, unduly excitable, irritable, and "difficult," and has perhaps suffered from cardiac troubles. A very common statement in the anamnesis is that there is intolerance for cocaine, as manifested on the extraction of a tooth. The general conclusion seems to be that, whatever part the thyroid and other internal secretion glands play in the setting up of the pathological process, injury to the nervous system is by far the most important etiological factor.

Exophthalmic goitre may follow acute diseases, such as typhoid, rheumatism, diphtheria, and especially influenza. Bialokur reports its occurrence in twenty-seven of 337 cases of pulmonary tuberculosis, and its stimulation in the early stages of the symptoms of the latter disease has sometimes led to an erroneous diagnosis. It is not uncommon in chlorosis. McCarrison's (10) extensive researches in relation to endemic goitre, in the course of which he obtained good results from vaccines prepared from organisms isolated from goitre, suggest the possibility that the enlargement of the thyroid in exophthalmic goitre may also be due to some nonspecific infection.

Treatment. The treatment of cases of exophthalmic goitre is always difficult, and demands a maximum of good judgment on the part of the physician if he wishes to obtain a successful result without referring them to the surgeon for thyroidectomy. It is a mistake to assume that the condition is practically incurable by medical treatment, and after a careful study of its results in the hands of various writers, including Hale White (11) and Mackenzie (12), Solis Cohen (13) concludes that there is a reasonable prospect of recovery in about seventy-five per cent. of the cases, which is about the same proportion as that allotted to surgery in the hands of competent surgeons. At the same time there is no doubt that for some cases surgery is imperative, and in this respect each case should be judged on its own merits. Whatever the treatment adopted, it is exceptional for all the symptoms to disappear completely, but most authorities agree that we are justified in speaking of cure if the general condition and strength are maintained, and the symptoms are relieved to such an extent that the patient is able to resume her ordinary occupation.

The brief account which has been given of the various hypotheses in regard to the causation of the disease makes it obvious that in the treatment it is essential to adopt measures tending to reduce excessive vascularity of the gland, thereby diminishing secretion and the tendency to hyperthyroidism. With this object in view it is absolutely necessary to secure for the patient the most complete bodily and mental rest obtainable under the circumstances, thus removing the stimulating effect on the thyroid of exercise and excitement. In some of the slighter cases a simple rest and isolation cure alone may relieve the symptoms, and if persevered in for some considerable time result in subsidence of the enlargement of the gland. During the first stage of the treatment rest should be so complete that it should not even be disturbed by the administration of medicaments. The length of time during which it is advisable for the patient to remain in bed varies in accordance with the progress of the case. The best guide in this respect is the condition of the pulse. When it has remained regular and practically normal for three or four weeks, the patient may be allowed to rest on a sofa in the room for an hour or so daily, and subsequently increase the amount of exertion very gradually day by day. The benefit of the rest cure

is likely to be greater if it is possible to take it in the country, preferably in a bracing climate, and away from the ordinary surroundings of the patient.

Defective nutrition is commonly associated with this disease, and therefore a liberal and nutritious diet, similar to that often recommended in pulmonary tuberculosis, is frequently indicated. Foods rich in extractives should be avoided, the diet consisting chiefly of milk and cereals, together with fruit and the more easily digested vegetables. It should be borne in mind, however, that gastric hyperacidity is present in not a few of these cases, and that under such circumstances it is advisable to forbid acid fruits.

Medicaments. As regards the medicaments which have been recommended, their name is legion, and the most contradictory opinions are given by different writers as to the efficacy of most of them. Opinions differ as to the advisability of giving hypnotic drugs, such as veronal, sulphonal, and trional. Some writers recommend them for the purpose of procuring sleep and lessening excitability, while others emphasize the fact that in neurotic cases of this description the drug habit is easily formed, and not so easily given up. Williams (15) thinks that the only sedative drug permissible is aspirin. The benefit sometimes derived from belladonna is due rather to its property of controlling glandular secretion than to its sedative qualities.

Of the bromides the only preparation which has been found useful is hydrobromide of quinine, which is highly recommended by Miller (16), Forschheimer (17) and others. Bumsted states that with it he has been able to cure several cases which had previously proved refractory to all other forms of treatment, including operation, and that one of its advantages is that it can be taken for months together without bad effects. In my own practice I have found that the most effective drug treatment is the administration of this preparation in the form of capsules or cachets, each containing five grains of hydrobromide of quinine and one grain of ergotin, the dose being given three times daily.

Leigh Watson (18) reports beneficial results from the injection of one to four c. c. of a thirty to forty per cent. solution of quinine and urea in fifty cases of exophthalmic goitre, the dose being repeated every third day. Two severe cases remained free from symptoms eighteen months after the last injection, and sixteen have been free from symptoms for one year.

On the assumption that exophthalmic goitre is more common in districts in which the water is deficient in lime, treatment by the administration of calcium salts has been recommended. Campbell (19) states that during the last eighteen months he has been in the habit of treating his cases in this way, and has had better results than from any other form of medication. He does not suggest that it should be the only treatment, but that it should be combined with any other form of treatment selected. He gives a dose of ten grains of chloride of calcium daily.

In view of the liability to digitalis toxemia in toxic conditions of the thyroid, many writers emphasize the desirability of avoiding the use of this and other cardiac drugs, except in cases in which special indications, similar to those in organic disease of the heart are present. Weiland (20) points out that such indications are absent in the cases in which some surgeons recommend a dose of digitalis before operation,

and that they should therefore be included in the category in which the drug is contraindicated.

Organotherapy. Some writers state that they have obtained satisfactory results from administration of extract of the thymus gland, but the reports as regards treatment by organotheraphy, including the administration of thyroid substance, are on the whole not very favorable, and do not compare with the brilliant results obtained in cretinism and myxedema from organotherapy. Serum from thyroidectomized sheep and milk from thyroidectomized goats are sometimes used in the forms of preparations known as rodagen, thyroidectin, and antithyroidin, and have been found useful in some cases.

Roentgen Rays. The fact that X-rays are known to have a selective effect upon glandular tissue, justifies the assumption that their use may be beneficial in exophthalmic goitre, and they have accordingly been extensively used, both alone and in combination with surgery. Satisfactory results are reported by several writers, and Kienbock (21), Nagelschmidt (23) and others go so far as to say that no operation for this condition should be undertaken without preliminary treatment by X-rays, and that if this procedure were universally adopted it would be likely materially to reduce the operative mortality of exophthalmic goitre. Belot (23) is of the opinion that even in the so called abortive cases in which struma is absent, the rays have a favorable influence on excessive and dysfunction (deficient or perverse function) respectively of the glands of internal secretion, even if these abnormalities are not associated with appreciable enlargement. Dr. Dawson Turner (24) reports successful cases, in which application of the X-rays was followed by diminution in the size of the thyroid and subsidence of the symptoms. This retrogressive process was associated with atrophy of the secretory epithelium and interstitial and extracapsular fibrosis.

Radium Treatment. Clinical experience shows that many cases do not respond satisfactorily to any of these methods, and in these refractory cases I have found the employment of radium to be of decided benefit. Abbe, of New York, first used radium successfully in exophthalmic goitre, and his favorable experience of its results has been repeatedly confirmed by other writers. The experiments of Victor Horsley and Finzi (25) show that the most constant changes after the application of radium affect the blood and lymph vessels. My own clinical experience shows that, when applied over the thyroid, the more penetrating radium rays diminish the vascularity and reduce the secretion of the gland.

Dawson Turner, who has had very favorable results, thinks that radium has two definite advantages when compared with the X rays, i. e., 1, the possibility of giving definite doses; 2, the fact that it can be applied without noise or excitement, while the patient remains in bed.

The following cases will serve as examples of the benefit to be derived from the use of radium rays in exophthalmic goitre:

Case 1.—Mrs. M., aged thirty-one years; married; two children. Five years before coming to me, she noticed enlargement of the thyroid and had used local applications, probably iodine, with no effect. A month before she consulted me the growth had increased to such an extent that it was spreading to the lateral lobe. She had suffered from difficulty in breathing, and discomfort on speaking or swallowing. Recently her appetite had been bad, and she had felt tired, nervous, and disinclined

for work. On examination, the thyroid was found to be definitely enlarged and pulsating, especially its middle and right lobes, the neck being fifteen inches in circumference. The pulse rate was 88, accelerated on slight exertion. The condition appeared to be an early stage of exophthalmic goitre.

Three thyroidectin tablets, each containing five grains, were given daily, and in addition a radition of 100 mg. hours was given with a large radium plaque. A week later the circumference of the neck had diminished to fourteen inches, the pressure symptoms were better, and the patient felt better. Five weeks after the beginning of the treatment the neck was thirteen inches in circumference, the tumor had almost disappeared, the patient no longer complained of nervousness, and she has remained well ever since.

Case 2.—A young unmarried woman of twenty-one years had for a year been so nervous, excitable, and changed in disposition that her parents feared for her mental condition. A physician was consulted, but apparently he did not suspect the real nature of the disease. When she first came under observation, she was in a highly nervous condition, with marked tremor, cardiac rapidity, and enlargement of the thyroid, the circumference of the neck being fourteen inches. The treatment adopted was rest in bed, with an ice bag applied over the heart, and the administration thrice daily of a quinine hydrobromide capsule (five grains hydrobromide, ergotin, one grain). The thyroid gland was subjected to a heavy exposure to radium rays. Three months later the neck was only twelve and one-half inches in circumference, and the tachycardia and nervous symptoms had disappeared. Further radium treatment has since been given; she has now continued well for more than two years, and has been able to resume her normal life.

Case 3.—In this case, in a young woman, the circumference of the neck was sixteen and three-quarter inches. When first seen, signs of hyperthyroidism were not marked, there being slight tremor, but no tachycardia. She was not treated by absolute rest until severe tachycardia suddenly developed, the pulse rate going up to 160, when she was at once put to bed with an ice bag over the precordia. Radium was applied to the thyroid, and in three months the neck measured only twelve and one-half inches, the pulse rate at the same time becoming normal. She has remained well ever since, that is for over three years.

Case 4.—A married woman, aged thirty-five years, was referred to me by Dr. G. W. Smith, of North Bay. She had suffered for the previous five months from exophthalmic goitre, which developed six months after the removal of the ovaries. The thyroid gland was only slightly enlarged, but there was well-marked tremor, and the pulse rate was 140. She had been treated at home by rest in bed, suitable diet and medication, together with other ordinary recognized measures of treatment, but without result. As a last resort she was sent to me for radium treatment. I prescribed absolute rest in bed, with an ice bag over the precordium, and the administration thrice daily of hydrobromide of quinine (five grains, with one grain ergotin). In addition heavy radiation was instituted of the thyroid. The improvement was marvellous. Within two weeks the pulse rate had dropped to 75, and nervousness had almost entirely disappeared. The patient was kept under observation for six weeks, when she went home in apparently normal health. When seen again, about six months later, there had

been no return of the symptoms of hyperthyroidism, and I am informed that she continues well.

Case 5.—A girl of nineteen years, referred to me by Dr. Clarke, of Bowmanville, Ontario, who presented the typical picture of Graves's disease. The thyroid was fairly prominent, the circumference of the neck being fourteen and one-half inches. There was well marked exophthalmos, the pulse rate was 120, and the patient was very nervous. No benefit had resulted from all the ordinary measures of medical treatment, which had included the administration of hydrobromide of quinine and ergotin and of Moebius's serum, together with absolute rest for some months. She was kept in bed with an ice bag over the precordium, the quinine and ergotin being continued. In addition an exposure of seventy mg. hours of radium was given over the thyroid. She went home and was not seen again for five weeks. At the end of this time the pulse rate was still 120, but the circumference of the neck was reduced to thirteen inches. She was further radiumized, and when seen again, two months later, the pulse rate had dropped to 76, tremor had disappeared, and the exophthalmos was scarcely noticeable.

This patient was last seen in September, 1915, when she had improved sufficiently to be able to do light housework. The neck measurement remained thirteen inches, and the pulse rate was 80. The effect of radium in this case was most marked, as before its employment no improvement whatever had resulted in the patient's condition.

Case 6.—An unmarried woman, aged forty-five years, manifested symptoms of exophthalmic goitre in March, 1915. She complained of a "sick nervous feeling," and marked tremor. The pulse rate was 130. There was considerable improvement after a rest cure, but the slightest exertion brought about a return of the symptoms. She first consulted me early in October, 1915, when there was definite exophthalmos and tremor, the pulse rate rising to 120 on the least exertion. There was marked prominence of the left lobe of the thyroid, the neck measuring fourteen and one-half inches. Hydrobromide of quinine and ergotin were given, with an ice bag over the heart. Radiation was applied over the thyroid. After receiving the treatment she returned to her home in the country. When next seen, on November 2nd, she looked and felt very much better. The neck measurement was half an inch less, the pulse at no time exceeded 90, and the nervousness had disappeared. Further radiation was given.

In January, 1916, the patient returned for observation. The pulse was only 76 a minute, even and regular. The left lobe of the thyroid was still somewhat prominent, but the symptoms of hyperthyroidism had disappeared completely.

Case 7.—In this case all the recognized symptoms of severe hyperthyroidism were present, with the exception of enlargement of the thyroid gland. The patient was a married woman of twenty-seven years. Protuberance of the eyes was first noticed after an attack of influenza in the spring of 1913, and subsequently dyspnea and palpitation. During the following winter, the symptoms diminished somewhat in severity, but after an attack of tonsilitis in March, 1915, she began to have attacks of vomiting, suffering from palpitation, and was easily excited or startled the action of the heart becoming very rapid. In June, 1915, she was kept in bed for five weeks, when her pulse became normal. When seen in August, 1915, there was no enlargement of the thyroid,

but the eyes were prominent, and the pulse ranged from 84 to 120. Radiation was given over the thyroid, and in October she reported that she was much better, the pulse was steadier, and she had gained in weight. In January, 1916, after further treatment, she was able to take short walks and do light house work without disturbing the pulse, nervousness had nearly disappeared, and instead of having become a confirmed invalid she had become a normal young woman.

Hydrotherapy.—Hallevorden (26), whose article is based on 100 cases, has had excellent results ffrom the hydrotherapeutic method recommended by von Winternitz, which consists of packings and demibaths. The treatment is always agreeable to the patient, and the pulse usually goes down on the application of the packing. With it he gives daily cold applications to the neck and back, and also to the heart if cardiac symptoms are prominent. The avoidance of exhausting and depressing baths is advisable. In slighter cases benefit is often derived from indifferent, salt or gaseous baths of comparatively low temperature. If fever is present, it should be treated by tepid full baths or cool full baths, in accordance with the indications. Tight collars and tight lacing should always be avoided.

Conclusion.—In conclusion, I should like to refer briefly to the psychological aspect of the condition, and its significance in relation to treatment. In view of the fact which is now generally accepted, that injury of some kind to the nervous system is—even if not a primary factor—at least a very important factor in the etiology of exophthalmic goitre, and that as a rule symptoms referable to it predominate in the clinical picture, it follows that one of the essential objects in our treatment is to endeavor to relieve these nervous symptoms, and that therefore psychotherapy plays an important role. This being so, it is obvious that it is highly desirable that physicians who have not had much experience with neurotic and neurasthenic people, and consequently do not understand them and have no sympathy with them, should refrain from undertaking the medical treatment of cases of this kind, in which the psychic element is such an important feature.

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REVIEWS AND ABSTRACTS.

H. K. Pancoast, M.D. and William Alfred Sawyer. The Results of the Use of Radium for Two Years at the University Hospital. The Penna. Med. Journ. No. 10, XIX, pp. 800-801, July, 1916. Abstract of a report presented before the Philadelphia County Society, May 24, 1916. "The report is made with the full realization that the results to date are but tentative; time alone will develop their ultimate value. A few of the cases were treated with radium and with the X-ray; many were inoperable; in others operation and radium were employed conjointly. We have classified our cases as (1) those cured or apparently cured; (2) those benefited; (3) those not benefited. It is felt that there is a class of cases in which a definite cure can be effected; another in which it is safe to say only that an "apparent cure" has resulted or that the patient is benefited. We have not in this summary taken into account the dosage or frequency of radium applications as that is of importance chiefly to the radiotherapeutist, and as radium in the hands of any but those making a study of it is dangerous we have properly left out the methods and technic of application. The report deals with 240 cases, both benign and malignant lesions, treated from May, 1914, to May, 1916; Sixty-nine have been treated by Dr. John G. Clark in the department of gynecology and it is from his report that we quote his results; all of the others were treated by Dr. H. K. Pancoast. Of these 240 patients treated, there are "apparently cured," or cured, 96; benefited, 57; not benefited, 35; refused treatment or failed to return, 30; dead, 22."

"It is worthy to note that 30, or approximately 13 per cent. of the patients treated, failed to return or continue treatment for one cause or another. Some did not realize the need of subsequent application, the first treatment having benefited them to such an appreciable extent. Others, because of the slowness of the treatment, became discouraged and ceased taking treatment. Gynecologically, the therapy is at present only a palliative measure. The two-year period is not yet over. Dr. Clark's results are good and show splendid possibilities. It is obvious that in some cases radium is of undoubted value. Local lesions may be eradicated, symptoms relieved, life prolonged, or the individual restored to normal health. There is yet much to know concerning its use and perhaps an ever-widening field of efficacy."

"Dr. Henry K. Pancoast, in discussing: In the treatment of malignancy by any means now known it is essential to consider, in connection with the case, every known means of treatment adapted to the case and then to select the particular method or methods most efficacious. One objection made to the radium treatment has been that cases have been treated promiscuously and without good judgment. The results

of the radium treatment in carcinoma of the rectum have been disappointing, in the vagina, far better. In cavities or canals constantly functionating, the use of radium or of the X-ray is not so satisfactory as in those which are not. A preliminary colostomy is essential to the satisfactory treatment of a rectal case with radium. When the lesions are low down metastasis is more probable than when located higher up. In lesions of the mouth methods to remove sloughing tissue are indicated in combination with the radium treatment. In the treatment of brain tumors and of many growths of the neck I think radium can be used to better advantage in cross-firing than can roentgen radiation. Radium is of particular advantage in the treatment of naevi and in growths of rather superficial venous supply; care must be taken to prevent sloughing and scarring. In growths with deeper and pulsating vessels other methods than radium are necessary."

"Dr. John G. Clark: I think the future will demonstrate that we shall have fewer, perhaps, of operable cases in the sense of the desire to operate in the more extensive cases, than in the past, and, therefore, shrinkage of the number of surgically operable cases, and an increase of the number which will use radium. In the last two years of our work radium has been a special boon to many of the cases within the inoperable zone. The relief of hemorrhage and of pain and the healing of local ulcerated areas have amply demonstrated its value as a palliative remedy. We have had two or three cases in which the results would seem to be almost miraculous. We must, however, wait until the expiration of the given time before we can speak definitely of results."

"Dr. Charles H. Frazier: It would seem that tumors of the brain should lend themselves to some such treatment as that of radium, since so many are inoperable from one cause or another. Tumors of the brain in many instances grow very slowly, and if we have at our command a remedy which will keep the growths under control we have a very useful means of prolonging life. I shall refer only to the six cases of malignant tumors of the cerebellum which Dr. Sawyer mentioned in his paper. One case was a fibrosarcoma, believed to be inoperable. A 50 mg. tube of radium was introduced in May. Silk was tied to the tube which was removed through the wound. The patient returned in July for a second treatment but failed rapidly. As Dr. Pancoast has said, fibrosarcoma does not respond well to radium. A second case interested us very greatly; in operating to examine the cerebellar pontine angle no evidence of the tumor could be found. A cerebrospinal fistula had developed at the site of the wound, the subarachnoid space became infected and the patient died of meningitis a year after the original operation."

"This leaves four cases in which the patients are still alive. The first case is that of a child, ten years of age, who when first seen was bedridden and almost blind. The lesion was a deep-seated cerebellar tumor. After exploratory incision operation was thought to be impossible and radium treatment was instituted, and the patient returned twice for treatment. The child is now able to be up and about the house and is greatly improved, although there are still marked symptoms of cerebellar disturbance. A second case is that of a woman of forty years, operated upon two years and two months ago, when a tumor in the right cerebellar fossa was removed. Several applications of the X-ray and radium were made; the patient entirely recovered and has

had no recurrence. This result I attribute to the use of the X-ray and radium combined. The third case is that of a boy of fifteen brought from the South. The tumor was exposed in the right cerebellar pontile angle and the case regarded as hopeless. Two tubes of radium, 35 and 50 mg. were inserted and allowed to remain from 12 to 8 o'clock the following morning. The patient was bedridden and almost blind from optic atrophy. He was brought back to the University Hospital a year after operation for a second treatment of radium, when he had but few symptoms of cerebellar disorder. I communicated with the boy's mother a few days ago and learned that he now goes to business and apart from his blindness, which might have been prevented by earlier operation, he seems to be entirely well. The fourth case is that of a young woman of thirty-five, treated seven months ago for inoperable cerebellar tumor. Staggering has largely disappeared and the patient is able to walk by herself and has gained in weight and strength. I am reminded of a fifth case in which I believe that for the time being radium had some effect. While this is but a short series the results certainly justify a continuance of radiotherapy in this particular field."

* * * * *

Henry Schmitz, M. D., (Chicago). The Action of Gamma Rays of Radium on Deep-Seated Inoperable Cancers of the Pelvis. Bulletin of the Chicago Medical Society, XV., No. 42, June 24, 1916.

Dr. Henry Schmitz said that radium therapy of malignant tumors in any part of the body demands the discussion of the following points: 1. The technic of the application of radium. 2. The evidence of the histological changes caused in the tumor tissue. 3. The clinical results. It also must include employment of all accessory means, which will facilitate the action of radium. 4. The application of the massive Roentgen rays. 5. The use of surgical procedures to facilitate or aid the intensity of the gamma rays of radium.

The technic of the application of radium must consider: 1. The amount of radium element used. 2. The method of screening. 3. The extent of the time of exposure of the rays and the tumor mass. The quantity of radium necessary to destroy growths that reach two to three centimeters into the uterine, rectal, vesical and pelvic cellular tissues, should be at least fifty milligrams of radium element. If the capsule cannot be brought into direct contact with the tumor, then a sufficient intensity of the rays must be obtained by the use of the larger amounts of radium element.

The experiments in the human body were carried out in recurrent breast cancers, characterized by the formation of multiple nodules. A nodule was removed under local anesthesia and subjected to a microscopic examination to determine its pathological nature. Then the gamma rays of fifty milligrams radium element were applied for four hours to a given nodule, for six hours to another nodule, for eight hours to a third one, for ten hours to a fourth, for twelve hours to a fifth one, and so forth. After ten to fourteen days, *i. e.*, when the latency of the action of the gamma rays reaches its height, the nodules were removed. He noted particularly the distance of the growths from the skin surface. The removed tissues were subjected to microscopic examinations. In this

manner he repeatedly demonstrated the fact that the gamma ray of 50 milligrams radium element destroyed carcinoma tissue within a distance of one centimeter from the skin surface after a continued application of twelve hours, *i. e.*, 600 milligram hours or milligramage.

The schedule of a course of radium applications, based on these facts, is as follows: The duration of a course of treatment varies from twelve to 108 hours, when fifty milligrams of radium element are employed, depending on the extent of the cancer into the tissues. The course is divided into seances of twelve to twenty-four hours, the interval between the sittings being from twelve to thirty-six hours. He endeavors to invariably give the total amount estimated within one week.

If 100 milligrams of radium element are used, then the duration of the treatment is correspondingly reduced. Should it be impossible to apply the radium directly to the tumor mass, then longer exposures or larger amounts must be used to correct the reduction of the intensity of the rays caused by the increase in distance. The law of inverse squares must be applied in consideration of these facts.

He has, fortunately, seven cases in which an abdominal panhysterectomy was performed after a clinical cure of the cancer by the use of radium rays was obtained.

He gave the clinical results of thirty-five inoperable, twelve recurrent and fifteen operable uterine carcinomata; seven inoperable, and three operable rectal cancers, and five inoperable, two recurrent and one operable carcinomata of the bladder. The total number is eighty. They were treated between April 1, 1914, and April 1, 1916.

The results of the radium treatment differ, depending, first, on the organ involved, and, second, on the stage of the disease. The prognosis is best in vesical cancers, less favorable in uterine malignant growths and least favorable in rectal carcinomata. The value of the treatment varies, depending on the operability, inoperability or recurrence of the disease. The time elapsed in all the cases enumerated is too short to permit a discussion of the curative action of radium.

Conclusions: 1. The therapeutic action of radium depends on the use of a correct technic, which must be based on a careful physical examination of the patient and the physical properties and the biologic action of the element.

2. The use of massive Roentgen rays, according to multiple field and crossfire methods, in conjunction with radium therapy, to destroy metastases, is an imperative necessity.

3. Certain surgical procedures must be used in radium therapy to assist the action and facilitate the application of the rays.

4. The action of X-ray on cancer tissue is specific and suggests positive proof of the possibility of destroying malignant tumors by the application of radium.

5. The results of radium therapy in inoperable and recurrent cancers surpass those of any other known therapeutic agent.

6. The prophylactic use of radium rays in operable carcinomata increases the percentage of operability and probably the efficacy of the operative procedudes.

DISCUSSION.

Dr. A. J. Ochsner said he has had an opportunity of observing the work Dr. Schmitz has been doing with radium, and up to the first of May Dr. Schmitz has treated eighty of his cases of inoperable carcino-

ma. Of this number, there were sixty-two uterine, ten rectal, and eight vesical cancers. Clinically, he is absolutely certain that there are now living among these eighty a number who would have died months ago if radium treatment had not been resorted to. There were cases in which there was such a degree of invasion of the surrounding tissues as to make the destruction of the cancerous tissue impossible by any other means than radium, and a certain number of these patients are alive today, consequently it was worth while to have made use of this method. As the work progresses he observes a considerable improvement in the results, because at the beginning of this treatment the technic had not been so thoroughly worked out as at present.

All the histological specimens he had seen and examined personally and the impression one gets is that radium has a very intense beneficial effect upon cancer.

Dr. Carl Beck said the paper of Dr. Schmitz covered very accurately the present status of radium therapy; that his results are better than those of most observers, due to the fact, perhaps, that Dr. Schmitz carefully studies and selects his cases. He would object to the use of the word cured in the statistics of Dr. Schmitz. Dr. Ochsner had not used the term cured. Observation shows the effect of radium upon the cancer cells, but before we can speak of a cure we have to be much more certain than the doctor could be of his results. Carcinoma is not a local disease, and when we have inoperable carcinoma of the uterus we cannot speak of a local disease any more. All those who have had experience have observed carcinoma away up in the abdomen and in distant regions, and, therefore, any local effect that radium might have upon the cancer would be limited to great improvement locally and not universally. We could not speak of a definite cure. While he has observed great improvement in many cases, he could not say that he had ever seen demonstrated a cure except in some of the superficial epitheliomata and superficial rodent ulcers which have been regarded by many practitioners as non-malignant.

Dr. Blaine said the term cured, as pointed out by Dr. Beck, should be used very sparingly when we speak of results in the treatment of carcinoma, whether it be by the Roentgen ray, radium, or by other methods. In his experience with a large number of these cases, he is frequently asked, What is your percentage of cures? There are none. He has no percentage of cures, but we undoubtedly do benefit more than half of our cases, putting it conservatively.

Dr. Schmitz, in closing, said he did not want to convey the impression that he was speaking of the curative action of radium. He did not refer to the results as clinical cures. It is impossible to speak of an anatomical cure until five years have elapsed and the patient has remained well. Patients suffering with generalized carcinoma cannot be treated satisfactorily with radium or X-ray, and for that reason only those parts of cancer would necessarily be influenced by the radium to which the radium rays can be sent.

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Joseph B. Bissell, M.D. (New York). Bone Sarcoma Treated by Radium. New York Med. Journ. CIV, No. 1, pp. 3-5, July 1, 1916. (Patients and photographs presented before the Surgical Section,

Academy of Medicine, May 5, 1916). "These patients are presented as examples of results which sometimes follow the application of radium to sarcomatous tumors of the long bones."

"Case 1. W. T., nineteen years old, had been in several hospitals and clinics and under various treatments before coming under my care. He first noticed this growth nearly two years ago. He had had experience with considerable doses of X-rays as well as Coley's serum. Two pathologists had reported upon specimens taken from the tumor. They concurred that it was an osteosarcoma of the spindle cell variety, arising from the periosteum. According to the skiagraph the growth involved the whole circumference of the left femur at its middle third. The early pictures before treatment with radium presented the characteristics of a sarcoma. The last picture, taken since the application of radium, is reported by Dr. Meyer, of Bellevue Hospital's X-ray staff, to resemble a chronic periostitis. The patient had in addition a severe radium burn on the limb, extending deeply into the muscle of the inner side. This burn extended almost completely around the leg. It had taken a long time to heal and was still troublesome. Considering, however, that the tumor had practically disappeared under treatment, the patient was not making more than the ordinary complaints about the inconvenience of the condition. At the beginniug of the radium treatment, the circumference of the leg over its largest point was 53.25 cm., the right leg at the same point being thirty-five cm. for contrast. The affected leg over the site of the original tumor is now 40.25 cm. in circumference, and part of this measurement is probably due to the swelling of the soft parts from the radium burn. This boy had rather large doses of radium, and for a comparatively long time. The average amount used was about 400 mgm., and for the first four or five times the exposure was twenty-four hours in length each time. Various kinds of screens were used and every endeavor was made to protect the skin from burns. There was a space screen of an inch and a half from his skin to the material screens, which consisted of from three to five mm. of rubber, and two mm. of brass or lead, depending upon the special applicator used, beside the original silver container, one mm. in thickness, and the glass tube containing the radium."

Photographs show the improvement from the time the patient came under Dr. Bissell's care up to the present, when the last photograph was taken. A skiagraph shows the improvement in the condition of the bone between the same dates.

"Case II. Isador S., five years old, first noticed a tumor in the upper third of the left humerus about a year ago. X-ray pictures, soon after, showed evidences of a rarefied swelling of the bone. Later on this was seen to be a sarcomatous infiltration, subperiosteal in origin. The diagnosis was confirmed by the examination of a section by the pathologist. The following measurements were made in May, 1915, before applying the radium treatment:

"Over the greatest size of the tumor, twenty-two cm.; at its lowest portion, seventeen cm.; one inch above the greatest diameter, eighteen cm. Fifty mgm. of radium were applied around the bone in five containers of ten mgm. each. They were applied at equal distance points and remained on about two hours. They were applied close to the skin with three mm. lead screens covered with 0.5 mm. rubber. In a week's time this application was repeated, also two weeks later. The measure-

ments taken early in July after these three applications were as follows: Over greatest diameter, eighteen cm.; below fifteen cm.; and above sixteen cm. Nothing more was done until the following September, when two similar applications were made, two weeks apart; the patient in the meantime continuing to improve until at this time there was very little difference between the arms. The child's general health was good. He had no pain or trouble of any kind relating to this tumor. Following the foregoing treatments there were no radium burns and the tumor almost disappeared. Palpation of the arm at the site of the tumor showed that there remained several irregular ridges parallel with the long axis of the bone. Late in November the tumor began to grow again; the patients general condition became affected; he had slight chills, rise of temperature, loss of appetite, complained of pains in his arms and chest, and seemed otherwise ill. An X-ray picture of his chest showed what was thought to be metastatic deposits in the mediastinum. In order that he might get the benefit of further radium applications, he was taken into the Radium Sanitarium and one hundred and fifty mgm. of radium was applied to his arm for twelve hours. Preceding this, a section was taken of the tumor, the pathologist reporting that it was a spindle cell sarcoma. A second X-ray interpretation showed it to be subperiosteal. Another skiagraph, several weeks later, showed no such pathological condition in the chest as described above."

"The tumor is still rather marked, although somewhat smaller than when the patient first came to the hospital. Several applications of radium of 150 mgm. each, for twelve or fourteen hours at a time, have not decreased it very much. He has a pronounced necrosis about an inch in diameter, of the soft parts of the arm, due to an X-ray burn. His general health at present appears to be about normal."

"These two patients are taken for contrast. One has apparently entirely recovered from the growth, the other has improved but slightly. The pathological condition, the character and position of the tumors, as well as the treatment carried out, are similar, yet the results are apparently opposite; although it may be said for the little boy five years old, that under a former series of radium applications the tumor has also practically disappeared. In spite of this seemingly poor result I believe that radium properly applied is the correct treatment. The only alternate is amputation at the shoulder joint, with almost certain early return of the tumor, either in the scar or in some other part of the body."

"At the Radium Sanitarium and laboratories we are constantly learning more about the pathological, histological, chemical, and clinical results of the action of radium and other agents upon the various malignant tumors in the human body. In some of its aspects malignant disease seems general or constitutional rather than local. It would not be surprising if in a short time such a theory proved to be a fact, and new growths, now regarded as limited, surgically removable, and curable, were recognized, after all, as only symptoms or indications of a widely disseminated dyscrasia not permanently eradicable by the knife alone."

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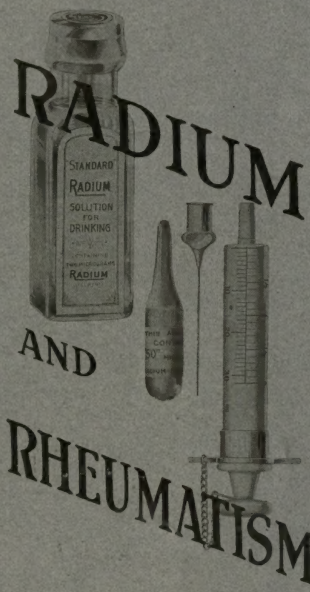

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